Roller Compaction Technology for the Pharmaceutical Industry

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INTRODUCTION

The pharmaceutical industry uses granulation methods to enlarge and densify small powder particles into larger ones. This improves powder flow so that the material can be processed effectively and efficiently further into solid dosage forms. There are two pharmaceutical methods of granulation, wet and dry. Wet granulation methods are widely described in the literature; for example, Encyclopedia of Pharmaceutical Technology (*Granulations*) is solely devoted to this technology.[1]

Dry granulation processing does not use moisture or heat to process powder into densified granules. In the pharmaceutical industry, there are two methods of dry granulation: slugging and roller compaction. Very little has been written about pharmaceutical dry granulation technology. Its contemporary use in the industry is about 50 yr–60 yr, beginning in the late 1940s. However, its popularity has risen in the last 20 years in parallel with the increased research for new efficacious active drug molecules in the pharmaceutical industry. These new active molecules cannot be processed so easily using wet and heat granulation processing steps, because of their chemical fragility and sensitivity. Therefore, this pushes the necessity for the use of dry granulation processing techniques to advance new sensitive active solid dosage forms in the 21st century.

BACKGROUND

Briefly, in dry pharmaceutical granulation processing, the powder particles are aggregated under high pressure, typically 30 bar–70 bar pressure. Particulate matter can be aggregated when compressed at high pressure because of bonding forces developed by the direct contact between the solid surfaces. The high pressure serves to improve the contact area between the surfaces and thus the overall bonding strength. Sometimes, a binding agent is needed to provide additional bonding strength. Later in the chapter, there is more about the kind of excipients used in roller compaction formulations to aid the manufacturing of pharmaceutical products.

In the pharmaceutical industry, dry granulation processing in the 1950s–1970s favored a process called slugging. This process design consisted of feeding powder into a large compression machine, such as a Stokes D3 type compression machine, where the powder was compressed into large tablets or slugs, typically in the order of 1-in. diameter with a tablet gauge of about 0.25 in. The tablet slugs were subsequently milled by a separate sizing machine to an appropriate particle size distribution, and further processed into pharmaceutical capsules, powder for oral suspensions, sachets, or tablet dosage forms. The slugging process is still used today by only a few manufacturing firms that have old pharmaceutical or over-the-counter formulation processes. Today, modern pharmaceutical formulation processes introduced into the Americas, Western Europe, Australia, and parts of Asia do not use this kind of dry granulation equipment in newly developed formulations. The slugging machine process is a relic of the past in the 21st century of modern pharmaceutical technology; roller compaction is the key technology to dry granulation processing of the future.

Some characteristics are described briefly about the slugging process to complete the technology information for the reader. The slugging process is externally influenced by raw material feed properties such as powder cohesiveness, density, flow characteristics, and powder particle size distribution. The slugging machine's design characteristics such as machine type, feed hopper, feed frame, die diameter and tooling features, compression speed, and slugging pressure also influence the slugging process and the final product properties. In general, the key processing operational aspect of slugging is to maintain a uniform powder fill weight into the dies during the dynamics of the slugging process. This assures the best chance to

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manufacture uniform powder slugs and ultimately, uniform densified granules. The compression-slugging setup is a key essential to maximizing the slugging throughput and minimizing the hopper feed frame and die powder flow problems associated with the process. Slugging compression is normally performed at 4 tn–6 tn hydraulic pressure, at a rate of 10–30 turret revolutions per minute. The specific machine tonnage, turret speed, and roll dwell time required for the process are dependent on the powder blend's physical properties, the tooling configuration, machine parts, and ultimately the slug specifications. Typical slugging machine output ranges from 30 kg hr^{-1} to 50 kg hr^{-1}. Slugging machines are not instrumented with modern devices to control their performance. There are numerous disadvantages with the slugging technology in the pharmaceutical industry as listed in Table 1.

BENEFITS OF ROLLER COMPACTION

This chapter identifies key aspects of roller compaction technology. Unlike the slugging process technology, roller compaction technology is well suited for dry granulation agglomeration in the era of modern development of active pharmaceutical ingredients and the design of modern pharmaceutical plants. The increasing scale of manufacturing pharmaceutical products worldwide and the need for high processing rates, together with increased levels of good manufacturing practices necessitate controlled dry granulation processes with as few processing steps as possible. This has been accomplished by instrumenting roller compactors to automate and control the mechanical process. Roller compaction technology plays a very important role in providing competitive cost control, safety, and quality products in the pharmaceutical industry. Key roller compaction benefits observed in the pharmaceutical industry are identified in Table 2.

Table 1 Disadvantages of slugging

Single batch processing	Excessive air and sound pollution
Frequent maintenance change-overs	Increased use of storage containers
Poor process control	Increased needs of manufacturing space
Poor economics of scale	Increase of logistics
Low manufacturing throughput per hour	More energy and time required to produce 1 kg of slugs than 1 kg of roller compact

(From Ref.[2], courtesy of the *Handbook of Pharmaceutical Granulation Technology*.)

A number of these attributes, best technology practices and features, were rated for their industrial and pharmaceutical importance and reported by Miller and Sheskey in 2001.[3] Ultimately, today's roller compaction technology offers a continuous process with better process controls, manufacturing efficiencies, and environmental protection than an archaic slugging process technology.

PREFACE: POWDER GRANULATION AND COMPACTION

Powder granulation is a process of powder size enlargement that incorporates small particles into larger ones. The definition of granulation comprises a range of different size enlargement methods that can be classified as either dry or wet. In wet methods, a suitable liquid is used to agglomerate the small powder particles into a mass. The wet mass is subsequently dried and sized for further down-stream processing needs. Wet granulation methods have been the most widely used powder granulation technology in the production of pharmaceutical products, particularly in modern pharmaceutical manufacturing.

The chief reasons to granulate powders for the manufacture of pharmaceutical dosage forms are described by Kristensen and Schaefer:[1]

- To improve powder flow properties for dosage filling and compression processes
- To eliminate wet granulation induced degradants and to improve product stability
- To prevent active product ingredient from segregating
- To reduce bulk volume thereby minimizing storage and enhancing transport
- To reduce potential environmental and safety hazards

Kristensen and Schaefer provide ample literature references in their chapter in the Encyclopedia of Pharmaceutical Technology about granulation size enlargement methods:[1] Capes,[4,5] Pietsch,[6,7] Sherrington and Oliver,[8] Kapur.[9] Others also referenced about wet granulation technologies: Kristensen and Schaefer,[10] Lindberg,[11] Fonner, Anderson, and Banker,[12] Anderson, Banker, and Peck,[13] and Ghebre-Sellassie.[14]

COMPACTION THEORY

The bonding forces in a dry aggregate are important to granulation properties such as granule integrity, flowability, friability, density, compressibility, and size for down-stream manufacturing process steps.[1] Rumpf and coworkers described the bonding mechanisms

Table 2 Advantages of roller compaction

Simplifies processing	Uses less raw materials
Eliminates aqueous and solvent granulating	Eliminates water-induced degradants
Facilitates powder flow	Improves process cycle time
Uses minimal energy to operate	Prevents particle segregation
Requires less man-hours to operate	Facilitates continuous manufacturing
Improves drug dosage weight control	Improves content uniformity
Reproduces consistent particle density	Does not require explosion-proof room or equipment
Produces good tablet and capsule disintegration	Produces a dry product that is process scaleable

(From Ref.[3], courtesy of the *Handbook of Pharmaceutical Granulation Technology.*)

occurring during dry granulation as a mixture of van der Waals' forces, mechanical interlockings, and a recombination of bonds established between freshly created surfaces and solid bridges, created because of partial melting and solidification during compression.[1,5]

A general theory describes particle bonding related to roller compaction in the *Handbook of Pharmaceutical Granulation Technology.*[2] The process of dry granulation relies on interparticulate bond formation. Granule bond formation is characterized in different stages, which usually occur in the following order:

1. Particle rearrangement
2. Particle deformation
3. Particle fragmentation
4. Particle bonding

Particle rearrangement occurs initially as powder particles begin filling void spaces. Air begins to leave the powder blend's interstitial spaces, and particles begin to move closer together. This action increases the powder blend's density. Particle shape and size are key factors in the rearrangement process. Spherical particles will tend to move less than other-shaped particles because of their close initial packing to one another. Particle deformation occurs as compressional forces are increased. This deformation increases the points of contact between particles where bonding occurs and is described as plastic deformation.[2]

Particle fragmentation follows as the next bonding stage. This occurs at increased compression force levels. At this stage, particle fracturing creates multiple new surface sites, additional contact points, and potential bonding sites. Particle bonding occurs when plastic deformation and fragmentation happen. It is generally accepted that bonding takes place at the molecular level, and this is due to the effect of van der Waals' forces.[2]

When powder granules undergo an applied force or stress, a stress force is released from the granules. The granules attempt to return to their original shape or form; this is described as *elastic deformation.* A deformation, which does not totally recover after the stress is released, is a *plastic deformation.* Elastic and plastic deformations can occur simultaneously, but one effect usually predominates.

Parrot identified that three theories of compressional bonding exist: mechanical, intermolecular, and liquid-surface film. Mechanical bonding purports that individual particles undergo elastic, plastic, and brittle deformation. Bonding of this nature occurs because particle surfaces intertwine, forming mechanical bonds. Intermolecular theory identifies that there are some unsatisfied surface ions that have a potential need to bond to one another. Under pressure, intermolecular forces become pushed together close enough so that van der Waals' forces can act to consolidate particles. The liquid-surface film theory identifies that bonding occurs because of the existence of a thin liquid film. The thin liquid film is generated from pressure induced by the energy of compression. This mechanism acts as a bonding agent promoting mechanical strength and an enlarged particle.[15] Very little information has been written about this last theory.

Dehont et al. provided a simplified approach to roller compaction theory.[17] They described that powder granules move through stages in the feed area. The material is drawn into the gap by rubbing against the roll surfaces. The densification that occurs in this area is particle rearrangement. At this stage, the speed of the powder is slower than the peripheral speed of the rollers. Fig. 1 represents compactor rolls in the horizontal plane; powder is pushed vertically downward into the compaction area.

Note in Fig. 1, α is the nip angle and β the material in volume space. The material is located in the compaction area between α and the horizontal axis (Fig. 1). At this stage, the material undergoes additional compaction forces. The particles undergo plastic deformation and are bonded. Dehont's team noted that nip angle varies according to the material characteristics of particle size and density and the angle is about 12°.[17] They defined the neutral angle, γ, which corresponds to the point where the pressure applied by the rollers

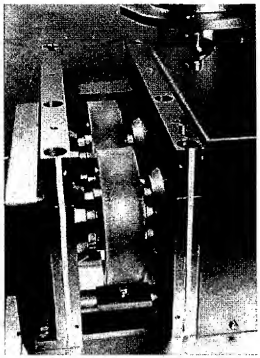

Fig. 21 Fixed rolls on two bearing blocks, rolls are concave. (Courtesy of Bepex-Hosokowa Co.)

A specially designed compression feed screw and upper arm assembly are shaped to closely conform to the inner wall of the feed hopper. The feed screw (usually non-cylindrical) has uniquely pitched edges. The feed screw design features and gravity aid to drive the powder-stock into the compaction area. There is no vacuum deaeration system. Predensification and deaeration occur in the screw feed region during operation.

Monitoring and controlling the roll speed and force and the feed screw speed and torque are adjusted through PLC for process controls. Prebreaker and flake crushers are attached sizing features. CIP capability exists.

Vector Co. compactor (Fig. 22) consists of cantilevered rolls that are mounted on a horizontal plane; one roll is fixed, the other floats. The feed screw designs are specially tapered and consist of non-cylindrical and cylindrical shapes. Monitoring and controlling the roll force and speed, gap distance, as well as the feed screw speed and torque can be adjusted through PLC for process controls. There is no vacuum deaeration system. Predensification and deaeration occur in the screw feed region during operation. The Vector compactor rolls can be water cooled. The feed screw design features and gravity aid to drive the powder-stock into the compaction area.

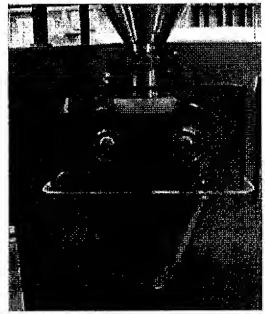

Fig. 22 Cantilevered compactor with one fixed and floating rolls, no vacuum deaeration, sizing device not attached. (Courtesy of Vector Co.)

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